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10/078,805	02/18/2002	James S. Stefely	51737US019	7639

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EXAMINER	
FISHER, ABIGAIL L	

ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/078,805	STEFELY ET AL.	
	Examiner	Art Unit	
	ABIGAIL FISHER	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *12 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42,44-52,55 and 57-87* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42,44-52,55 and 57-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/20/08 and 12/04/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Amendments/Remarks filed on November 12 2008 is acknowledged. Claims 1-41, 43, 53-54, 56, 81-82 and 88-188 were/stand cancelled. Claims 47-49, 52, 61-66, 68-73, 79-80, 83-86 are amended. Claims 42, 44-52, 55 and 57-87 are pending.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Information Disclosure Statement

The information disclosure statement filed August 20 2008, specifically B1, fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered.

The information disclosure statement (IDS) submitted on 12/04/08 was considered by the examiner.

Claim Objections

The objection of claims 81 and 82 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is

withdrawn in light of Applicants' cancellation of the claims in the reply on November 12 2008.

The examiner would like to remind applicants of proper claim presentation. Specifically 37 CFR 1.121 (c) (4) indicates that no claim text shall be presented for any claim in the claim listing with the status of canceled or not entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 78 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

The specification, while being enabling for free base and pharmaceutically acceptable salts of particular drugs, does not reasonably provide enablement for solvates or solvates of salts. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Formal, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

The nature of the invention, relative skill, and breadth of the claims

The instant invention is directed to formulations comprising a drug.

The complex nature of the claims is greatly exacerbated by the breath of the

[1] As pointed out by the court in In re Angstadt, 537 F.2d 498 at 504 (CCPA 1976), the key word is

claims. The claims encompass any solvate or solvate of a salt of the drugs listed. The relative skill of those in the art is high, that of an MD or PHD.

The state and predictability of the art

As illustrative of the state of the art, the examiner cites Grant et al. Grant et al. (Advanced Drug Delivery Reviews, 2001) indicates that predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice is both complex and difficult. All compounds respond differently to possible formation of hydrates. Therefore Grant et al. indicates that generalizations cannot be made for a series of compounds and their respective hydrates (page 19, section 3.4).

The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for how to form a solvate, or solvate of a salt. Due to the vastness of compounds classified as drugs, one of ordinary skill would undergo undue experimentation in deducing which compounds can actually form solvates or solvates of salts as well as which solvent can actually be utilized to form such a solvate.

Thus, in the absence of working examples there is no showing that the instant compounds will form solvates or solvates of salts. Since it is clear that merely bringing the compound into contact with water does not result in a solvate, additional direction or guidance is needed to make them and the specification has no such direction or

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"undue", not "experimentation".

guidance.

The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed compounds can form solvates and solvates of the salts of the compounds as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 47-49, 52, 61-66, 68-73, 80 and 83-86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is **withdrawn** in light of Applicants' amendments filed on November 12 2008 removing the term about and arguments regarding the upper and lower limits of claims 65 and 66.

Claims 42, 44-52, 55 and 57-87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Instant claim 42 recites that the formulation results in discrete, non-film forming particles. However, as evidenced by EP 0521455 A2, poly lactic acid and glycolic acid

polymers and more generally biodegradable hydroxycarboxylic acid polymers are known in the art as film forming polymers in aerosol preparations (page 2, lines 38-43). Therefore, it is unclear how the instant application particles are non-film forming as the polymers taught in EP '455 are the same as instantly claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 42, 44-51, 55, 67, 74-77, and 79-87 under 35 U.S.C. 103(a) as being unpatentable over Patton (US Patent No. 5607915, cited in the Office action mailed on 10/9/07) is **withdrawn** in light of Applicants' arguments filed on November 12 2008 that the polymer is not dissolved in the propellant.

The rejection of claims 42, 44-51, 55 and 57-60, 67-68 and 76-87 under 35 U.S.C. 103(a) as being unpatentable over Boyes et al. (US Patent No. 5384133) in view of Baker (US Patent No. 4670250) is **withdrawn** in light of Applicants' arguments filed on November 12 2008 that the polymer is not dissolved in the propellant.

The rejection of claims 74 and 75 under 35 U.S.C. 103(a) as being unpatentable over Boyes et al. in view of Baker and in further view of Patton is **withdrawn** in light of Applicants' arguments filed on November 12 2008 that the polymer is not dissolved in the propellant.

The rejection of claims 52, 61-66 and 69-73 under 35 U.S.C. 103(a) as being unpatentable over Boyes et al. in view of Baker and in further view Hunter et al. (US Patent No. 5716981) is **withdrawn** in light of Applicants' arguments filed on November 12 2008 that the polymer is not dissolved in the propellant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 42, 44-52, 55 and 57-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duan et al. (WO 94/21229, cited on PTO Form 1449) as evidenced by Takada et al. (US Patent No. 6117455).

Applicant Claims

Applicant claims a sustained release aerosol formulation comprising: a propellant, a therapeutically effective amount of a drug, and a sufficient amount of a biocompatible polymer, at least four times the amount of the drug on a weight to weight basis, dissolved in the formulation so as to provide for sustained release of the drug; wherein the sustained release formulation results in discrete, non-film forming particles upon delivery, and wherein the formulation is contained in a metered does inhaler for oral and/or nasal inhalation, and wherein the biocompatible polymer comprises at least one chain having a plurality of units of the formula:

$-[X-R^1-C(O)]-$ wherein:

R^1 is an independently selected straight chain, branched chain, or cyclic organic group containing 1-6 carbon atoms optionally containing carbonyl groups, oxygen atoms, thio groups, or caternary nitrogen atoms that links the X group to the carbonyl group; and each X is independently oxygen, sulfur, or caternary nitrogen.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Duan et al. is directed to a medicinal aerosol formulation containing a particulate drug and a dispersing aid derived from a hydroxyacid, a mercapto acid, or an amino acid (abstract). The invention proves an aerosol formulation comprising a dispersing aid, a propellant, and a particulate drug. The dispersing aid comprises a compound comprising a chain of units of the formula ($XR_1C(O)$) wherein R_1 is moiety that links X to the carbonyl group and X is independently an O, S, or caternary nitrogen (page 3). Examples of the chain include hydroxyacids such as a hydroxycarboxylic acid (page 4,

lines 20-21). It is taught that when X is O R_1 is preferably a straight chain, branched chain, or cyclic alkylene or alkyenylene containing from 1 to 6 carbon atoms (page 5, lines 10-15). Chain length of the polymer is generally less than 100, preferably between about 3 and about 70. It has been found that with lactic acid based dispersing aids, length of about four or more are particular preferred for use with the propellant HFC-227 while chain length of about 6 or more are particularly preferred for use with HFC-134a (page 7, lines 12-30). Embodiments of the invention include polymers comprising units derived from glycolic acid and lactic acid (page 12, lines 31-33). It is preferred that the dispersing aid is soluble in a propellant composition (page 12, lines 1-2). The dispersing aid is in an amount effective to stabilize the formulation relative to an identical formulation not containing the dispersing aid. The particular amount of the dispersing aid that constitutes an effective amount is dependent upon the particular dispersing aid, the particular propellant and on the particular dug used and such amounts can readily be determined by those skilled in the art with due consideration of the factors set forth above. Generally the amount of dispersing aid can be present in an amount of about 0.001 to about 1 part by weight based on 100 parts by weight of the propellant (page 13, lines 15-35) It is taught that in aerosol formulation particles can be prepared in respirable size and then incorporated into a suspension formulation containing a propellant. Alternatively, formulations can be prepared in solution form in order to avoid the concern for proper particle size in the formulation (page 1, lines 27-33). Dispersing Aid B had a molecular weight of about 700 (page 20-21). The drug administered is preferably micronized. Suitable drugs include analgesics,

bronchodilators, albuterol, etc. The amount of the drug will generally range from about 0.02 to about 2 parts by weight based on 100 parts by weight of the propellant (pages 13-14, lines 17-35 and 1-4). Examples 35-38 contain the dispersing aid in an amount of 0.05% and the drug in an amount of 0.03% by weight which is a ratio of polymer to drug of 1.67 to 1. Other components such as lubricants, surfactants and cosolvents such as ethanol can be present in the formulation (page 15, lines 14-16). Propellants specifically taught include chlorofluorocarbon propellants (page 15, lines 5-12). It is taught that administration can be dosed via a conventional value such as a metered dose valve (page 14, lines 4-17).

As evidenced by Takada et al., the polydispersity of a polymer is defined as the value of weight average molecular weight divided by the number average molecular weight (column 9, lines 33-36). The polydispersity of dispersing aid B is 1.29 (page 21) and dispersing aid F is 1.15 (pages 23-25). It is taught that the molecular weight distribution of a product dispersing aid can be adjusted and optimized by using methods well known to those skilled in the art (page 18, lines 10-13).

Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)

Duan et al. do not exemplify formulations comprising the polymer in an amount at least four times the drug or specify specific release profiles of the drug. However, Duan et al. do teach amounts of the drug and propellant that overlap those instantly claimed and the drugs, propellants, and polymers taught are the same as instantly claimed.

Finding of Prima Facie Obviousness Rationale and Motivation
(MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to manipulate the ratio of polymer to drug of the invention of Duan et al. as Duan et al. teach ranges that are suitable for both the propellant and drug. "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969). Duan et al. teach that amount of the polymer can be about 0.001 or about 1 and amount of the drug can be about 0.2 to about 2. Therefore, it would have been obvious to one of ordinary skill in the art to vary the amount of drug and polymer to determine the optimum combination. It is noted that about 1 includes amount greater than 1, which would read on instant claim 44.

Regarding, the instant claims functional limitation in terms of release rate, Duan et al. is silent. However, Duan et al. teach the same polymers, same drugs and same propellants in amounts that overlap those instantly claimed. Since these are all the same, it is the examiner's position that the product would necessarily have the same profile as instantly claimed. Note MPEP 2112.02 (1I): "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705,709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize the drug in either suspension form or in a micronized

suspension. One of ordinary skill in the art would have been motivated to utilize either a suspension or solution as Duan et al. teach that either one is suitable. While a suspension may be preferred by Duan et al., it is taught that in order to avoid the concern for proper particle size in the formulation a solution can be utilized. Therefore, it is well within the skill of one of ordinary skill in the art to formulate either a suspension or a solution. Furthermore, depending on the characteristics (i.e. solubility) of the particular drug chosen the formulation may necessarily be a suspension or a solution depending on the solubility of the particular drug in the chosen propellant.

Regarding the claimed chain length, Duan et al. teach amounts that overlap those instantly claimed. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. **See MPEP 2144.05 [R-5]**

Regarding the claimed polydispersity, Duan et al. exemplify dispersing aids which have a polydispersity of less than 1.2. Furthermore Duan et al. teach that the molecular weight distribution of a product dispersing aid can be adjusted and optimized by using methods well known to those skilled in the art. Therefore, it would have been obvious to one of ordinary skill in the art to adjust and optimize the molecular weight distribution based on the teachings of Duan et al.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting/Terminal Disclaimer

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The provisional rejection of claims 42, 44-52, 55 and 57-87 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 10327200 is **withdrawn** in light of applicants' arguments that the excipients covered in '200 do not overlap with those instantly claimed.

The rejection of claims 42, 44-52, 55 and 57-87 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 8- of U.S. Patent No. 7186402 in view of Baker et al. is **withdrawn** in light of Applicants' filing of a terminal disclaimer on November 12 2008.

The terminal disclaimer filed on November 12 2008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the

expiration date of US Patent No. 7186402 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claims 42, 44-52, 55 and 57-87 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-36 and 39-41 of U.S. Patent No. 5569450 in view of Duan et al. (WO 94/21229). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims overlap in scope.

The instant application claims sustained release aerosol formulation comprising: a propellant, a therapeutically effective amount of a drug, and a sufficient amount of a biocompatible polymer, at least four times the amount of the drug on a weight to weight basis, dissolved in the formulation so as to provide for sustained release of the drug; wherein the sustained release formulation results in discrete, non-film forming particles upon delivery, and wherein the formulation is contained in a metered does inhaler for oral and/or nasal inhalation, and wherein the biocompatible polymer comprises at least one chain having a plurality of units of the formula:

$$-[X\text{-}R^1\text{-}C(O)]-$$ wherein:

R^1 is an independently selected straight chain, branched chain, or cyclic organic group containing 1-6 carbon atoms optionally containing carbonyl groups, oxygen atoms, thio groups, or caternary nitrogen atoms that links the X group to the carbonyl group; and each X is independently oxygen, sulfur, or caternary nitrogen.

Patent '450 claim a medicinal aerosol formulation comprising a dispersing aid comprising a compound comprising a chain of units of the formula $–X-R_1-C(O)-$, A propellant and a therapeutically effective amount of a particulate drug. Species of the compound for the units include glycolic acid, trimethylene carbonate, and lactic acid which are the same as instantly claimed. The average chain length is of six to 12. The aerosol canister is equipped with a metered dose valve. The dispersing agent is claimed in an amount from about 0.001 to about 1 part by weight based on 100 parts by weight of the propellant.

Patent '450 does not claim that the dispersing aid is present in an amount four times the drug. However this deficiency is cured by Duan et al.

Duan et al. teach that the amount of to utilized in aerosol formulations for oral or nasal inhalation from a convention valve such as a metered dose are from 0.02 parts to about 2 parts by weigh based on 100 parts of by weigh of the propellant (page 14).

It would have been obvious to one of ordinary skill in the art to combine the teachings of Patent '450 and Duan et al. and manipulate the amount of drug and dispersing agent. Patent '450 claims a particular amount of dispersing agent. Duan et al. teach amounts of drug that are suitable. It would have been obvious to one of ordinary skill in the art to vary the amount of drug and dispersing agent to optimize the ratio of dispersing agent to drug. "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969).

Regarding, the instant claims functional limitation in terms of release rate, Patent '450 claims the same polymers. Therefore, the same release rate would be present in Patent '450.

Therefore, the scopes of the copending claims overlap and thus they are obvious variants of one another.

Response to Arguments

Applicants argue that patent '450 does not disclose or suggest a key feature which is wherein the polymer is utilized in an amount at least four times more than the drug. Applicants argue that '450 teach amounts of polymers in smaller amounts that the instant application.

Applicants' arguments filed November 12 2008 have been fully considered but they are not persuasive.

While Patent '450 does claim a specific amount of the dispersant, it does not claim a specific of drug. It would have been obvious to one of ordinary skill in the art to look to the teachings of Duan et al. which teach the same drugs and teach amounts of drugs to incorporate and manipulate the amount of teach to determine optimum combinations of drug and polymer. Regarding the amounts of the polymer, the amount claimed is from about 0.001 to about 1. About 1 reads on all of the percentages instantly claimed.

Therefore, the rejection is maintained since applicant has not provided any persuasive arguments to overcome the rejection.

Claims 42, 44-52, 55 and 57-87 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 5725841 in view of Duan et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims overlap in scope.

The instant claims are set forth above.

Patent '841 claims a metered dose inhaler containing a formulation comprising a dispersing aid comprising a chain of units derived from hydroxyacid, an amino acid, a mercapto acid and a combination of any two more of the former; a propellant; and a therapeutically effective amount of a particulate drug. Hydroxyacid is a particular species instantly claimed. The chain of the formulation can contain between about 3 and about 70 units.

Patent '841 does not claim specific amounts of drug or dispersing agents. However this deficiency is cured by Duan et al.

The teachings of Duan et al. are set forth above. Duan et al. additionally teach that the same dispersing agent can be utilized in an amount from about 0.001 to about 1 part by weight based on 100 parts by weight of the propellant (page 13) .

It would have been obvious to one of ordinary skill in the art to combine the teachings of Patent '841 and Duan et al. and manipulate the amount of drug and dispersing agent. Duan et al. teach amounts of drug and dispersing agents that are suitable. It would have been obvious to one of ordinary skill in the art to vary the

amount of drug and dispersing agent to optimize the ratio of dispersing agent to drug. "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969).

Regarding, the instant claims functional limitation in terms of release rate, Patent '841 claims the same polymers. Therefore, the same release rate would be present in Patent '841.

Therefore, the scopes of the copending claims overlap and thus they are obvious variants of one another.

Response to Arguments

Applicants argue that patent '841 does not disclose or suggest a key feature which is wherein the polymer is utilized in an amount at least four times more than the drug. Applicants argue that '841 teach amounts of polymers in smaller amounts that the instant application.

Applicants' arguments filed November 12 2008 have been fully considered but they are not persuasive.

While Patent '841 does claim a specific amount of the dispersant, it does not claim a specific of drug. It would have been obvious to one of ordinary skill in the art to look to the teachings of Duan et al. which teach the same drugs and teach amounts of drugs to incorporate and manipulate the amount of teach to determine optimum

combinations of drug and polymer. Regarding the amounts of the polymer, firstly, '841 does not claim specific amounts. Secondly, the amounts taught by Duan et al. are from about 0.001 to about 1. About 1 reads on all of the percentages instantly claimed.

Therefore, the rejection is maintained since applicant has not provided any persuasive arguments to overcome the rejection.

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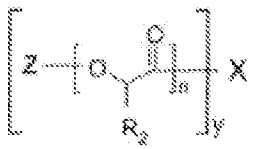
Claims 42, 44-52, 55 and 57-87 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-30 and 33 of copending Application No. 11816883 in view of Duan et al.

The instant claims are set forth above.

Copending '883 claims a formulation comprising a drug and a biocompatible polymer of the formula:



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Copending '883 claims that the polymer comprises units derived from D,L-lactic acid, which is the same as instant claimed. A further limitation is that the formulation comprises a propellant.

Copending '883 does not claim that the dispersing aid is present in an amount four times the drug. However this deficiency is cured by Duan et al.

The teachings of Duan et al. are set forth above.

It would have been obvious to one of ordinary skill in the art to combine the teachings of copending '883 and Duan et al. and manipulate the amount of drug and dispersing agent. Duan et al. teach amounts of drug and dispersing agents that are suitable. It would have been obvious to one of ordinary skill in the art to vary the amount of drug and dispersing agent to optimize the ratio of dispersing agent to drug. "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969).

Regarding, the instant claims functional limitation in terms of release rate, Copending '883 claims the same polymers. Therefore, the same release rate would be present in Copending '883.

Therefore, the scopes of the copending claims overlap and thus they are obvious variants of one another.

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

Applicants argue that since copending '883 was filed after the priority date of the present application a double patenting rejection requires a two-way obviousness analysis.

Applicants' arguments filed November 12 2008 have been fully considered but they are not persuasive.

The MPEP 804 indicates that unless the record clearly shows that the two applications could not avoid separate filings and the PTO controlled the rates of prosecution to cause the later filed claims to issue before the claims in an earlier application. It indicates that unless the record clearly shows administrative delay by the Office, the examiner may use the one-way obviousness determination.

Therefore, the rejection is maintained since applicant has not provided any persuasive arguments to overcome the rejection.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABIGAIL FISHER whose telephone number is (571)270-3502. The examiner can normally be reached on M-Th 9am-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Abigail Fisher
Examiner
Art Unit 1616

AF

/Mina Haghighatian/
Primary Examiner, Art Unit 1616